ABSTRACT

A method for constructing stable bioactive fusion proteins of the difficult to express tumor necrosis factor superfamily (TNFSF), and particularly members CD40L (CD154) and RANKL/TRANCE, with collectins, particularly pulmonary surfactant protein D (SPD) is described. Single trimers of these proteins lack the full stimulatory efficacy of the natural membrane forms of these proteins in many cases. The multimeric nature of these soluble fusion proteins enables them to engage multiple receptors on the responding cells, thereby, mimicking the effects of the membrane forms of these ligands. For CD40L-SPD, the resulting protein stimulates B cells, macrophages, and dendritic cells, indicating its potential usefulness as a vaccine adjuvant. The large size of these fusion proteins makes them less likely to diffuse into the circulation, thereby limiting their potential systemic toxicity. This property may be especially useful when these proteins are injected locally as a vaccine adjuvant or tumor immunotherapy agent to prevent them from diffusing away. In addition, these and other TNFSF-collectin fusion proteins present new possibilities for the expression of highly active, multimeric, soluble TNFSF members.